Exhibit 144

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Dear Mr. Slater:

This report is a supplement to my report dated July 6, 2021, providing further discussion of the failure by ZHP to conduct a reasonable risk assessment of chemical reactions and necessary testing with regard to the TEA with sodium nitrite quenching process, and Zinc Chloride process, resulting in the manufacture and sale of valsartan API and finished dose contaminated with NDMA and NDEA. All opinions are stated to a reasonable degree of scientific certainty.

In summary, ZHP (and its subsidiary Shanghai Syncores that developed the zinc chloride process in the laboratory) could have and should have identified the risk of formation of nitrosamines including NDMA and NDEA, and utilized that information to test for and identify, and then prevent the nitrosamine impurities in the valsartan API and finished dose sold by ZHP. This could have and should have been done during and after development of the processes, and throughout the time that ZHP manufactured and sold the contaminated valsartan with those processes.

As stated in my July 6, 2021 report, the processes were flawed from the outset because of the inclusion of chemical reactions that could foreseeably create nitrosamines in the API. Specifically, quenching the sodium azide with sodium nitrite (nitrous acid) in the presence of the product, which led to a reaction between foreseeably created secondary amines and the nitrous acid to create NDMA/NDEA. For example, the 1978 IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, established that the reactions forming nitrosamines including NDMA and the use of mass spectrometry to identify nitrosamines were well known. In this connection, Min Li confirmed that the reaction described in the IARC monograph, "the reaction of dimethylamine hydrochloride with sodium nitrite at an acidic pH yields NDMA," is what occurred in the zinc chloride process, and this chemical reaction was known since 1865. (Min Li 4/21/21 Dep. Tr. 458:13-465:11).

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In addition, ZHP has acknowledged the likely occurrence of cross-contamination of valsartan API manufactured with the zinc chloride and TEA with sodium nitrite quenching processes on shared production lines. "During the period when multiple processes co-existed in Workshop 2 and Workshop W02, equipment were cleaned as per corresponding cleaning procedure to control the residue of active substance from the previous batch when switch from one process to another. However, the residual NDMA and NDEA in the equipment after cleaning for process switch were not analyzed…Based on the analysis of the NDMA and NDEA data, the original equipment cleaning procedure applied might not be able to get rid of the NDMA and NDEA residue on the equipment completely." The Report also states that there was a risk of cross-contamination due to solvent recovery for the same reason: ZHP was not looking for NDMA or NDEA because they failed to perform a straightforward assessment of the chemistry. (ZHP Deviation Investigation Report dated November 5, 2018 (DC-18003, PRINSTON0075797, at 126-130). Min Li of ZHP confirmed: "the DEA [diethylamine] is a typical process impurity of TEA, so DEA would also, yeah, would react with the nitrous acid to perform NDEA." With regard to NDMA, "in some of the TEA raw material it may contain a trace amount of, you know, of dimethylamine, okay, so that's one root cause…for some of the, you know, product, they were manufactured, you know, using the share line, you know, with the zinc chloride valsartan." (Min Li 4/20/21 Dep. Tr. 77:8-80:16). Varied NDMA levels were found in the valsartan API produced in the East and West zones at Chuannan, per the TEA process DIR. ZHP identified factors that would impact the NDMA levels. This includes, "number 1, temperature when adding sodium nitrite; number 2, charging speed of hydrochloride acid; number 3, ph control at the end; and number 4, aqueous phased separation time during quenching." In this connection, ZHP recognized that there was "a lack of detailed description in the production processes." ZHP further stated, "Due to the inaccurate description of some of the parameters in the process, there might be likelihood of fluctuation between different workshops or different batches manufactured in the same workshop, which eventually led to the difference in the amount of residual impurities…the residual amounts of NDMA in valsartan API batches." (Peng Dong 4/2/21 Dep. Tr., 536:7-543:2). Assessment and understanding of the potential chemical reactions in each process would have required testing for NDMA and NDEA of each batch of drug product manufactured with both processes, whether due to the process or cross-contamination, and would have shown the presence of NDMA and NDEA in each batch, as applicable.

The readily available scientific knowledge and testing should have been applied to identify the NDMA and NDEA even after the processes were adopted. This should have been apparent to any organic chemist involved in the development or assessment of these processes. Once ZHP went forward with the processes after having failed to detect and prevent the nitrosamine contamination during the development of the processes, ZHP could have and should have identified the nitrosamine impurities before selling the API or finished dose with NDMA/NDEA impurities. The same scientific knowledge and principles I have discussed with regard to the development of the processes was equally available and could and should have been applied when the product was manufactured for sale. This would have been as easy as adding appropriate testing for NDMA and NDEA to the specifications, and

testing each batch of API and finished dose accordingly. The result would have been detection of the nitrosamines.

ZHP has stated that the detection of the nitrosamines was not possible since they had no knowledge of the potential or actual presence of the nitrosamines and did not possess the technological ability to identify these impurities. I disagree. The deposition testimony provides context for this issue. For example:

Jun Du testified with regard to the August 26, 2018 letter written by ZHP (and signed by him) to the FDA, stating in part that, "it is not the residual DMF that reacts with nitrous acid of the next step, but rather it is the trace amount of dimethylamine, an impurity/degradant of DMF that reacts with nitrous acid to form NDMA, which adds a further dimension over the current thinking, logic and strategy for the evaluation of potential genotoxic impurities. It is this extra dimension over the current industry practice that obscured us from foreseeing this impurity during the process change from triethylamine process to zinc chloride process." (Jun Du 5/28/21 Dep. Tr. 232:18-234:6).

In the November 28, 2018 FDA Warning Letter to ZHP, the FDA explicitly, and correctly disagreed with ZHP's position that this could not be known, "You also failed to evaluate the need for additional analytical methods to ensure that unanticipated impurities were appropriately detected and controlled in your valsartan API before you approved the process change….Your response states that predicting NDMA formation during the valsartan manufacturing process required an extra dimension over current industry practice, and that your process development study was adequate. We disagree. We remind you that common industry practice may not always be consistent with cGMP requirements and that you are responsible for the quality of drugs you produce." (ZHP01344159 (ZHP 213)). Dr. Li and Mr. Du agreed with the FDA that ZHP was "responsible for the quality of the drugs" produced by ZHP. (Min Li 4/21/21 Dep. Tr., 426:8-427:5, 430:11-434:10) (Jun Du 5/28/21 Dep. Tr. 247:17-250:22).

The FDA also stated in the Warning Letter, "You are responsible for developing and using suitable methods to detect impurities when developing, and making changes to your manufacturing processes. If new or higher levels of impurities are detected, you should fully evaluate the impurities and take action to ensure the drug is safe for patients." (Jun Du 5/28/21 Dep. Tr. 237:18-243:20). As stated in my prior report, the knowledge, technology, and methods to identify the NDMA and NDEA were readily available and should have been applied to identify the contamination, and this could and should have been done during development of the processes, and then again once ZHP began to manufacture valsartan with those processes for sale.

In this context, a draft of ZHP's deviation investigation report titled "Investigation Regarding an Unknown Impurity (Genotoxic Impurity)" stated that, "Due to insufficient extent and depth of process research at the early stage, as well as insufficient study and understanding of potential genotoxic impurities, only side reaction product and degradation

products were studied, and was unaware of the further reaction between degradation products and raw material." (Min Li 4/22/21 Dep. Tr. 528:5-531:4). This accurately describes the inadequate scientific risk assessment performed by ZHP, since the chemical reactions and means to test for the foreseeable creation of nitrosamines were well known and available. Scientifically reasonable process research, study and understanding of potential genotoxic impurities, would have resulted in recognition of the risk of creating the nitrosamine impurities, and testing that would have demonstrated the presence of these impurities. I know this from my own personal experience utilizing mass spectrometry to identify nitrosamines including NDMA beginning long before development of these processes in 2011, and the scientific literature including what is identified here and in my prior report, as well as in questioning of ZHP witnesses.

The focus on nitrosamines as potential human carcinogens began after the first demonstration of the carcinogenicity of dimethylnitrosamine in 1956 as outlined in my previous reports. The first report of nitrosamine contamination of food was published in 1968, and the first definitive evidence for the presence of dimethylnitrosamine in meat products in 1972.[1] This stimulated the development of reliable analytical methods for nitrosamines, layered on the existing knowledge base. A review published in 1976 notes the initial development of methods for the analysis of trace amounts of nitrosamines: "there is now no doubt that these compounds do occur in trace amounts in various environmental situations."[2] It goes on: "Recently a better standardization of the methodology, using gas-liquid chromatography and mass spectrometry, has yielded more reliable identification of the nitrosamines."

Fine et al reported the development of a highly sensitive and reliable nitrosamine-selective detector (the Thermal Energy Analyser, or TEA) in 1975.[3] Coupling of TEA to gas chromatography (GC-TEA) became the standard method for analysis of ultra-trace levels of nitrosamines. Thousands of products including pharmaceuticals were reliably analyzed and shown to contain trace amounts of nitrosamines (reviewed in Forman, D. and Shuker, D. Nitrate, nitrite and nitroso compounds in human cancer, *Cancer Surveys* 8: 205-487 (1989)), leading to international concern, further analyses, and mitigation efforts. Ultimately with the development of improved gas chromatography-mass spectrometry (GC-MS) methods and the wide availability of this instrumentation by the early 1980s, GC-TEA gave way to GC-MS which was even more reliable because of its ability to directly determine structural information from fragmentation patterns, information that was not available by GC-TEA. A review published in 1989 summarizes hundreds of analyses of nitrosamines in food.[4]

Thus, there is no doubt that the necessary technology and highly reliable methods for the analysis of nitrosamines in various settings were available from the 1970s. More recent analyses have confirmed the earlier data.

The international concern about the presence of these carcinogens in various settings gave rise to the widely attended and recognized International Agency for Research on Cancer conferences on nitrosamines which were held at various locations in the world from 1976-

1991. These meetings produced a series of books describing the research discussed at the meetings.[5]

In summary, nitrosamine contamination of food, drugs, and other products, and the reliable analytical methods to detect nitrosamines, have been known since the 1970s. Routes of formation of nitrosamines under various conditions have been extensively described in numerous publications and textbooks. Chemists using processes which involve the presence of nitrite and secondary amines should absolutely be aware of this huge body of literature, and utilize the widely available technology and methods to identify the nitrosamines resulting from these processes.

ZHP's witnesses acknowledged in their depositions that the chemical reactions were known and that mass spectrometry was available to identify nitrosamines starting before these processes were even developed. Dr. Li ultimately agreed that "the technology and the methodology was clearly available to identify the NDMA," as long as you "know what to look for" based on a risk assessment – which he confirmed is an ongoing process for the lifecycle of the drug. (Min Li 4/20/21 Dep. Tr., 230:9-19, 233:10-18).

Eric Gu also confirmed in his deposition that the 1978 IARC Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans" stated in part: "It has been known since 1865 that the reaction of dimethylamine hydrochloride with sodium nitrite at an acidic pH yields NDMA." (Eric Gu 4/5/21 Dep. Tr., 65:3-65:24). Mr. Gu was shown a 2009 article published in the scientific journal Tetrahedron Letters, titled: DMF, Much More Than a Solvent. The article states that "DMF decomposes slightly at its boiling point to afford dimethylamine and carbon monoxide, this reaction occurring even at room temperature in the presence of acidic or basic materials..." He agreed that DMF could decompose to yield dimethylamine, and this was known in the scientific community. (Eric Gu 4/5/21 Dep. Tr., 172:13-174:9, 183:12-21).

Min Li was shown scientific literature identifying the risk of formation of nitrosamines during his deposition. This includes a textbook first published in 1996 titled, Purification of Laboratory Chemicals, which stated that DMF could decompose at its boiling point to yield dimethylamine. (Min Li 4/21/21 Dep. Tr. 391:13-395:5). Another 2009 scientific article titled "N.N-Dimethylformamide: much more than a solvent," also stated that DMF could decompose to produce dimethylamine, and this article cited a textbook published in 1966. (Min Li 4/21/21 Dep. Tr. 411:19-413:22). In addition, an article published in 2010 by a group from Beijing University of Technology in the Journal of Physical Chemistry titled "Theoretical Investigation of N-Nitrosdimethylamine Formation from Nitrosation of Triethylamine," described the formation of NDMA from the reaction of dimethylamine and nitrous acid. This is what occurred here with the zinc chloride process. (Min Li 4/21/21 Dep. Tr. 414:2-416:12). Dr. Li also stated that this was the reaction that occurred in the zinc chloride process: "the zinc chloride process for the formation of NDMA, you know, was also under the acidic, you know, pH. So, yes, so from that perspective, yeah, they are consistent." He also confirmed that in 2011, "scientists would be aware of and have available to them" this information, as well as

the known availability and use of mass spectrometry to test for potential nitrosamines, as stated in the 1978 Monograph, "The principal techniques employed for the analysis of volatile N-nitrosamines [including NDMA] have been described in a recent publication…The relative merits of high- and low-resolution mass spectrometry are discussed, since use of mass spectrometry as a confirmatory technique is particularly important." (Min Li 4/21/21 Dep. Tr. 458:13-465:11). The literature discussed with the ZHP witnesses provides useful examples and is representative of information that was well known in the scientific literature and scientific community prior to and after the 2011 development of these processes.

The identification of the NDMA and NDEA would have been straightforward to anyone who was familiar with the chemical reactions in the manufacturing process, utilizing mass spectrometry. The location of the NDMA peak found on the chromatograms for the zinc chloride process has been identified by ZHP. For example, Min Li testified that there was a "little peak after the toluene peak" and stated, "And then in the sample injection, this peak turns out, if I remember correctly, to be n-butyl acetate, okay? So that's the peak - - that's the peak, you know, eluting after the toluene peak. Okay. So NDMA would elute on the shoulder, or sometimes may even completely co-elute with this peak." (Min Li 4/20/21 Dep. Tr. 25:16-28:22.). In addition, Qiangming Li confirmed that "[w]hen we used GC-FID for the testing, regarding the peak that appeared after toluene, the response of NDMA was pretty low." (Qiangming Li 4/14/2021 Dep. Tr. 168:17-20). The point is that taking into account the potential creation of nitrosamines should have led to the use of the GC-MS technology to identify the NDMA and NDEA.

A series of customer complaints was received by ZHP with regard to the unknown, or aberrant peaks on the chromatography. This included:

1. Ranbaxy/SunPharma on September 30, 2014 (Qiangming Li 4/14/2021 Dep. Tr. 130:7-170:11; ZHP01748896 (ZHP 260)).

2. Shanghai Pharmtech on November 20, 2014 (*Id.* at 177:22-199:20; ZHP01748905 (ZHP 264)).

3. SunPharma on November 17, 2016 (Qiangming Li 4/15/2021 Dep. Tr. 290:16-318:10; ZHP00405069 (ZHP 277); ZHP01313866 (ZHP 278)).

4. Vertex on December 21, 2016 (Qiangming Li 4/14/2021 Dep. Tr. 204:11-214:17; ZHP02630924 (ZHP 265); ZHP02630926 (ZHP 266).

5. Glenmark on December 29, 2016 (Qiangming Li 4/15/2021 Dep. Tr. 254:22-290:4; ZHP00496153 (ZHP 271); ZHP00496155 (ZHP 272); ZHP02118712 (ZHP 273)).

6. Aurobindo on August 23, 2017 (*Id.* at 343:21-372:9; ZHP02094739 (ZHP 281)).

7. Novartis on May 22, 2018 (*Id.* at 386:17-466:17; ZHP00405021 (ZHP 284)).

Testing with the available technology would have identified the NDMA and NDEA at every point during the period when these processes were used to manufacture the valsartan. Novartis did what ZHP should have done. Novartis investigated the unknown peaks to determine what was causing them, and identified the NDMA in ZHP API manufactured with the Zinc Chloride process. Of note, Novartis inquired of ZHP as to whether DMF was utilized in the zinc chloride process on June 7, 2018, as part of its investigation. (ZHP01390017). This was relevant information to be taken into account by anyone assessing the cause of the unknown peaks since dimethylamine was the degradation/decomposition product of DMF that then reacted with the nitrous acid to form NDMA. ZHP simply ignored or didn't understand this basic chemistry. ZHP failed to perform the same analysis despite knowing the details of the manufacturing process, and this illustrates the inadequacy of ZHP's risk assessment from the perspective of organic chemistry.

I have reviewed chromatograms for the zinc chloride process. The NDMA peak would not have been identifiable as NDMA on the gas chromatography alone, but as stated above if ZHP had been diligent and conducted a scientifically reasonable assessment, they would have recognized the need to test for NDMA, and they could have used the available technology to identify the NDMA peak. We have examples of the results that would have been obtained in the documentation of the testing performed after the disclosure of the NDMA in June, 2018. The September 1, 2018 ZHP Response to DMF Information Request Letter provides a series of chromatograms showing the methods used, and the identification of the NDMA peak. (ZHP00079913). There was nothing complex or difficult about what was done once they were looking for the NDMA (and ultimately NDEA). In another example, the July 20, 2018 Deviation Investigation Report titled: Investigation regarding a Suspected Genotoxic Impurity of Valsartan (ZHP00004363) contains images of the June 6, 2018 email and attachments from Kevin O'Mahony to Xavier and others at ZHP. The chromatograms show the NDMA peak, and the method used to identify the peak, (ZHP00004399-4402). This should have been identified from the outset and at every other point moving forward, including when Novartis and other customers submitted complaints and inquiries regarding unknown peaks, as listed above. In this context, the European authority documented that Novartis had shared its analytical method with ZHP in July, 2017, in rebutting ZHP's argument that it did not have that information until June 2018. (ZHP01862681 (ZHP 232)). Of note, and perhaps not a coincidence, the July 27, 2017 email written by Jinsheng Lin, Ph.D. confirming that there was NDMA in ZHP's valsartan API, caused by the quenching with sodium nitrite, was written during the same month.

The same analysis applies to the NDEA in the valsartan. For example, August, 2018 testing performed by ZHP shows the NDEA peak identified. (ZHP02733180).

When asked why Novartis discovered that an unknown peak was due to NDMA before ZHP, he acknowledged that ZHP was required to investigate the peak, but could not give an explanation, "it was not so easy to detect" and "it's quite a challenging work." (Eric Gu 4/5/21

Dep. Tr., 210:24-219:5, 236:24-237:8). As set forth above, identification was quite feasible and should have been accomplished from the start of development of these processes, through the entire time that the drug products were manufactured and sold. This could have been done at any point, and seeming to contradict ZHP's position that it did not know, the July 27, 2017 email accurately describes the presence of the NDMA and the root cause of quenching with sodium nitrite.

Mr. Gu was questioned about the aberrant/unknown peaks. He had no reasonable explanation for why, despite every batch demonstrating the "NDMA peak just after the Toluene peak on the chromatograms. . . nobody at ZHP realized that it needed to be tested and identified." Mr. Gu admitted that ZHP was aware of these peaks and "did whatever they can," however, "They are struggling, I guess, in the past." (Eric Gu 4/6/21 Dep. Tr., 333:21-335:19). Mr. Gu was not aware that ZHP customer Sun Pharmaceuticals complained of unknown peaks in November 2016, and was not aware that, according to the European Medicines Agency, ZHP did not directly compare the unknown peaks observed by Novartis to ZHP's own gas chromatography. Nor was he aware that Novartis had shared its GC-FID method for evaluating chromatogram peaks with ZHP in July 2017. (Eric Gu 4/5/21 Dep. Tr., 240:3-243:18).

To be clear, the pathway to identification of the NDMA and NDEA impurities continued to be straightforward after the valsartan containing NDMA and NDEA began to be marketed. ZHP could have and should have taken the steps described above from the time they began to sell the valsartan containing NDMA and NDEA until it was discovered by Novartis, with the aid of an outside laboratory in June 2018. The necessary information and technology was readily available the entire time.

In addition to the ease in detecting the NDMA and NDEA with available testing, if ZHP still determined to go forward with these processes, the simple step of extracting the product prior to the quenching could have been taken to prevent the NDMA (and NDEA in the TEA with sodium nitrite process) formed in the zinc chloride process during quenching of the sodium azide from contaminating the drug product. ZHP stated in one document that, "any formation of NDMA will not be carried over into the product," and, "This approach can be done without any change of manufacturing process." July 1, 2018 Investigation of the Source of this Impurity (NDMA) (ZHP01495188). ZHP also provided a detailed analysis at pages 29-35 of 236 of the November 5, 2018 Deviation Investigation Report (PRINSTON0075797), indicating: "After optimization, the ROS remains the same, the product in Valsartan Crude Step (Step 4) is separated before the addition of NaNO2 (and the subsequent addition of Hcl)…Therefore, the product in the organic phase has no chance to be contaminated by NDMA." This would not have changed the manufacturing process for the drug product or route of synthesis as recognized by ZHP, and would not have negatively impacted or introduced any risk to the identity, quality, purity, strength, or stability of the drug products, since the drug product would have been separated from and not been exposed to contamination by the genotoxic impurities created during the quenching step. The same could have been done with the TEA with sodium nitrite quenching process. In the alternative,

ZHP could simply have gone back to the original process that did not involve sodium nitrite quenching, as "no NDMA or NDEA will be formed in Tin process." (November 5, 2018 Deviation Investigation Report, at 68 of 236, PRINSTON0075870).

Eric Gu confirmed that ZHP modified the zinc chloride manufacturing process after the FDA became aware of the NDMA, and agreed that ZHP's, "solution was to quench the azide separate from the product so it wouldn't become contaminated with the NDMA," and, "GC-MS would be used to evaluate all peaks to make sure that they were not genotoxic impurities that needed to be controlled out of the product." (Eric Gu 4/6/21 Dep. Tr., 455:1-458:15). If the solvents presenting the risk of secondary amines and sodium nitrite quenching were to be used, this would have prevented contamination of the drug product, and this testing would have confirmed the lack of NDMA or NDEA; this was absolutely feasible and could and should have been done from development through the entire course of the manufacturing of the drug product if the same solvents and chemicals were to be used in the process.

The ZHP API and Finished Dose Nitrosamine Levels
Are Materially the Same and All Exceed the FDA Levels

Minli Zhang—ZHP's Director of Finished Dose Formulation Quality—testified that ZHP determined its APIs' nitrosamines carried over to the finished dose. (3/26/2021 Minli Zhang Dep. Tr. 509:15-17, 518:18-519:3). Ms. Zhang explained:

> In our investigation report, we compared the NDMA level in the API and the NDMA level in the finished dose products, and we found the results basically matched each other. Therefore, we decided not to test the NDMA level in the finished dose products anymore.
>
> We could simply calculate based on the NDMA level in the API, as well as the amount of API used, to come up with a probable level of NDMA in the finished dose products.

(*Id.* at 521:8-19). This is the chart from the deviation investigation report:

In order to qualify the impurity relationship between the dosage form and API, some batches of API and corresponding dosage form were choose at random to test this impurity by Quality Research Department (QR), the testing result is as below:

表 1：制剂成品及对应 API 批次检测结果列表

Table 1: testing result between dosage form batches and corresponding API

序号 SN	产品名称 Product Name	产品批号 Batch No.	产品规格 Strength (mg)	API 厂家批号 Vendor batch No. Of API	API 结果 Result for API	制剂结果 Result for dosage form
					NDMA 含量(ppm) Assay of NDMA (ppm)	
1.	缬沙坦片 USP Valsartan Tablets USP	341A18007	40	C5523-17-382	81.4	83.1
2.	缬沙坦片 USP Valsartan Tablets USP	342B17012	80	C5523-17-190	101.9	101.0
				C5523-17-191	101.7	
3.	缬沙坦片 USP Valsartan Tablets USP	343G17002	160	C5355-17-132	120.0	110.3
				C5355-17-133	104.5	
4.	缬沙坦片 USP Valsartan Tablets USP	344B17071	320	C5355-17-131	119.3	123.2
				C5355-17-132	120.0	
5.	缬沙坦氢氯噻嗪片 USP Valsartan HCTZ Tablets USP	609B18003	80/25	D5191-16-133	3.4	2.9
6.	缬沙坦氢氯噻嗪片 USP Valsartan HCTZ Tablets USP	611B17003	320/25	D5191-16-027	27.7	31.3
7.	缬沙坦氢氯噻嗪片 USP Valsartan HCTZ Tablets USP	611B17007	320/25	D5191-15-149	7.9	6.4

从上表数据分析，制剂产品与 API 的检测结果的差值接近(0.5~9.7ppm)。

Based on analysis above, the testing difference value of API and dosage form is almost the same (0.5-9.7ppm)

(ZHP00683571, 683578). As a result, ZHP stopped testing FD and blended the API levels to get the FD ones. (*Id.* at 520:22-523:19, 525:12-22 (discussing ZHP 189)). Hai Wang—the President of Solco—confirmed that the API and FD contained the same levels of nitrosamines. (3/10/2021 Hai Wang Dep. Tr., 116:3-118:23, 144:15-147:1). Prinston explicitly informed the FDA that "[i]t is confirmed that NDMA has been present in Valsartan drug substance (API) batches and carried to the drug product Valsartan," relying on the same test results as shown in the above chart. (PRINSTON00249966, 249967; ZHP00099424, 99441-42). ZHP concluded this analysis applied to NDEA as well. (PRINSTON0075797, 75977 (stating: "According to the previous raw material investigation, i.e. presence of diethylamine impurities in triethylamine hydrochloride, combined with the formation mechanism of NDEA, it should be the nitrosation of diethylamine impurities (in triethylamine hydrochloride) by nitrite to produce NDEA impurities, which is carried over into crude products, and finally remain in valsartan finished products.")).

As set forth in my July 6, 2021 report, testing by Teva and Torrent of its finished dose products manufactured using the ZHP contaminated valsartan API also established that the

levels of NDMA and NDEA all exceeded the limits set by the FDA. (TEVA-MDL2875-00546489 (TEVA 155); TORRENT-MDL2875-00005092; TORRENT-MDL2875-00369262; TORRENT-MDL2875-00072916; TORRENT-MDL2875-00366172).

Conclusion

The unreasonably dangerous contamination of valsartan drug products with NDMA and NDEA was easily avoidable, based on prevailing scientific knowledge and technology that existed before, during, and after the development and then commercial use of the zinc chloride and TEA with sodium nitrite quenching processes. The available knowledge and technology should have been applied to add straightforward testing for NDMA and NDEA of each batch of API and finished dose manufactured using the API manufactured with these processes, which would have revealed the presence of the NDMA and NDEA. The contamination of the drug product could have been prevented by extracting the product before quenching the sodium azide.

Stephen S. Hecht

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[4] Hotchkiss, J. H. Preformed *N*-nitroso compounds in foods and beverages. *Cancer Surv* **8**, 295-321 (1989).

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EXHIBIT A
Supplemental List of Materials Reviewed

ZHP Documents

1. PRINSTON00249966, August 27, 2018 Letter from Prinston to the FDA regarding ANDA 206083.
2. ZHP02326538 (ZHP 189).
3. ZHP00662283, Draft Investigation regarding an unknown impurity (Genotoxic Impurity) (ZHO 212).
4. ZHP01862672, Final GMP Inspection Report (ZHP 232).
5. ZHP01748896, Email Chain between ZHP and Ranbaxy (ZHP 260).
6. ZHP01748905, Email Chain between ZHP and Shanghai Pharmttech Co. Ltd. (ZHP 264).
7. ZHP02630924, Email Chain regarding Vertex (ZHP 265).
8. ZHP02630926, Chronology regarding Vertex (ZHP 266),
9. ZHP00496153, Email Chain regarding Glenmark (ZHP 271).
10. ZHP00496155, Chronology regarding Glenmark (ZHP 272).
11. ZHP02118712, Email Chain between ZHP and Glenmark (ZHP 273).
12. ZHP00405069, Email Chain between ZHP and Sun Pharmaceutical Industries Ltd. (ZHP 277).
13. ZHP01313866, Chromatograms from Sun Pharmaceutical Industries Ltd. (ZHP 278).
14. ZHP02094739, Email Chain between ZHP and Aurobindo (ZHP 281).
15. ZHP00405021, Email Chain between ZHP and Novartis (ZHP 284).
16. ZHP00099424, Meeting Information Package from Prinston regarding ANDA 204821.
17. ZHP01390017, Email Chain Between ZHP and Novartis.
18. ZHP01495187, Investigation of the Source of this Impurity (NDMA).
19. ZHP01344159, November 29, 2018 Warning Letter from the FDA to ZHP (ZHP 213).
20. ZHP01495186, July 1, 2018 Email Enclosing ZHP01495187, Investigation of the Source of this Impurity (NDMA).
21. ZHP02733180, Chromatogram and Results for NDEA in ZHP's valsartan
22. PRINSTON00002249, 1-2 Annex-3 NDMA for TEA Process by GC-MS
23. ZHP02365339, Valsartan Chromatograms
24. ZHP02364173, NDMA and NDEA test results for all batches of Valsartan in USDMF grade
25. ZHP00011368, Certificate of analysis for D5191-14-157M
26. ZHP00344175, Summary of Unspecified Peaks in Residual Solvents Method of Valsartan
27. ZHP00476862, Valsartan Impurities Profile Analysis Report (ZHP 220)

28. ZHP00021455, Study Report of Unknown Peak in Residual Solvent of Valsartan
29. ZHP01870977, Study Report of Unknown Peak in Residual Solvent of Valsartan
30. ZHP02214602-71, Novartis Documents
31. ZHP02633528-ZHP02633538
32. ZHP00405024-ZHP00405068
33. ZHP00380568-ZHP00380591
34. ZHP01748896-ZHP01748899-ZHP1748899 (ZHP 260)
35. ZHP00405069-ZHP00405070 (ZHP 277)
36. ZHP01320376-ZHP01320392 (ZHP 280)
37. ZHP00405021-ZHP00405023 (ZHP 284)
38. ZHP00359796-ZHP00359822 (ZHP 288)
39. ZHP02135008-ZHP02135025 (ZHP 289)
40. ZHP02173090-ZHP00371269 (ZHP 290)

Torrent Documents

1. TORRENT-MDL2875-00072916, Details of Finished good batches (USA market) manufactured at indrad with Huahai API having old ROS.
2. TORRENT-MDL2875-00366172, Valsartan: Impact assessment of NDMA.
3. TORRENT-MDL2875-00369262, Test Results
4. TORRENT-MDL2875-00005092, Details of Finished good batches manufactured at indrad with Huahai API having old ROS.

Deposition Testimony

1. Minli Zhang Deposition Transcript for March 22-26, 2021.
2. Eric Gu Deposition Transcript for April 5-6, 2021.
3. Qiangming Li Deposition Transcript for April 13-16, 2021.
4. Jun Du Deposition Transcript for May 27,-28, 2021.

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2. Ender, F. & Ceh, L. Occurrence of nitrosamines in foodstuffs for human and animal consumption. Food Cosmet. Toxicol. 6, 569-571, doi:10.1016/0015-6264(68)90292-7 (1968);
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4. Magee, P. N., Montesano, R. & Preussmann, R. in *Chemical Carcinogens. ACS monograph 173* (ed Charles E. Searle) 491-625 (American Chemical Society, 1976).
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6. Hotchkiss, J. H. Preformed *N*-nitroso compounds in foods and beverages. *Cancer Surv* **8**, 295-321 (1989).
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